| Notice of Allowability | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/009,782 | TAKEUCHI ET AL. | |
| | Examiner | Art Unit | |
| | Malgorzata A. Walicka | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--*

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Amendment filed Nov.26, 2003*.
2. ☒ The allowed claim(s) is/are *14-18 and 20-34*.
3. ☒ The drawings filed on *21 May 2003* are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

   **Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).**
9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____
4☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5☐ Notice of Informal Patent Application (PTO-152)
6☐ Interview Summary (PTO-413), Paper No._____ .
7☒ Examiner's Amendment/Comment
8☒ Examiner's Statement of Reasons for Allowance
9☐ Other .

The Amendment and Request for Reconsideration filed on Nov. 26, 2003 is acknowledged.

Claims 14 - 34 pending are the subject of this Office Action.

## DETAILED ACTION

### 1. Objections

The objection to the specification made in the Final Rejection is withdrawn, because the Sau3A1 restriction endonuclease site was recited by the original specification.

Objections to claims 19 are withdrawn because the claim has been amended.

### 2. Rejections

#### *2.1. 35 USC, section 112, second paragraph*

Rejection of claims 21 and 22 is withdrawn because the claims have been amended.

Rejection of Claim 19 and 20 for being indefinite is withdrawn because the claims have been amended.

Rejection of claims 14, 17-27 and 28-34 are moot in view of the amendment of the claims.

#### *2.2. 35 USC, section 112, first paragraph*

2.1.1. Lack of written description

Rejection of claims 14-16 and 18-27 is withdrawn because the term "expression" has been replaced with the term "activity".

***2.3. 35 USC section 102***

Rejection of claims 28, 29 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Wakayama et al. (Cloning and Sequencing of a Gene Encoding D-Aminoacylase from *Alcaligenes xylosoxydans* subsp. *xylosoxydans* A-6 and Expression of the Gene in *Escherichia coli*, Biosci. Biotech. Biochem, **1995**, 59, 2115-2119, included in IDS) is withdrawn, because the claims have been amended.

**3. Examiner's amendment**

Please amend the claims as follows.

(a) Please cancel claim 19.

(b) In claim 18 and 20 replace --D-aminoacylase–producing gene-- with --D-aminoacylase encoding nucleic acid sequence--.

(c) Change claim 14 to read:

14. An isolated microorganism comprising[:] a nucleic acid sequence that encodes the amino acid sequence of SEQ ID NO: 2, or a nucleic acid sequence from *Alcaligenes,* which encodes D-aminoacylase, which comprises the following sequence of restriction sites: Sal I, Bgl II and Pvu II[;], wherein said nucleic acid

sequences comprise SEQ ID NO:3 in the ninth position upstream from the first nucleotide in the start codon; [wherein] said microorganism is zinc resistant, and wherein the activity of D-amino acylase [from] encoded by said nucleic acid sequence in said microorganism is enhanced in the presence of zinc ion.

(d) 15. The isolated microorganism of Claim 14 that comprises a nucleic acid sequence that encodes the amino acid sequence of SEQ ID NO:2.

(e) 17. The isolated microorganism of Claim 14 that comprises a [D-aminoacylase gene] nucleic acid from *Alcaligenes* which encodes D-aminoacylase, the [expression] activity [of the gene product] of which is enhanced in the presence of zinc ion, [which encodes a D-aminoacylase,and which] wherein said nucleic acid comprises the following sequence of restriction sites Sal I, Bgl II and Pvu II, and comprises SEQ ID NO:3 in the ninth position upstream from the first nucleotide in the start codon.

(f) 28. An isolated nucleic acid sequence[:] which encodes the amino acid sequence of SEQ ID NO: 2, or which encodes a D-aminoacylase from *Alcaligenes*, [and] which comprises the following sequence of restriction sites: Sal I, Bgl II and Pvu II, wherein said isolated nucleic acid sequence comprises an upstream ribosome binding site comprising GAAGGA (SEQ ID NO: 3) in the ninth position upstream from the first nucleotide in the start codon.

(f) 32. An isolated nucleic acid sequence from *Alcaligenes* that encodes a D-aminoacylase and which comprises the following sequence of restriction sites: Sal I, Bgl II and Pvu II, [and] wherein said isolated nucleic acid sequence comprises an upstream ribosome binding site comprising GAAGGA (SEQ ID NO: 3)[.] in the ninth position upstream from the first nucleotide in the start codon.

Authorization for this examiner's amendment was given in a telephone interview with Applicants' representative T. Cunningham on January 16, 2004.

**4. Allowance**

Claims 1-18 and 20-34 are allowed. The following is the examiner reason for allowance.

Applicants disclosed a modified sequence of the D-aminoacylase gene from *Alcaligenes*, wherein a novel ribosome binding sequence of SEQ ID NO: 3 was introduced in the ninth position from the start codon of the gene. D-aminoacylase is an enzyme useful industrially for production of D-amino acids of high optical purity.

The closest prior art is the article by Wakayama et al. (Cloning and Sequencing of a Gene Encoding D-Aminoacylase from *Alcaligenes xylosoxydans* subsp. *xylosoxydans* A-6 and Expression of the Gene in *Escherichia coli*, Biosci. Biotech. Biochem, **1995**, 59, 2115-2119, which discloses a nucleic acid encoding SEQ ID NO:2. However, Wakayama et al. did not modify the gene by inserting a novel ribosome

binding site. The novel ribosome binding site sequence allows for an efficient expression of the *Alcaligenes* gene in E. coli. Although the Applicants' ribosome binding site sequence GAAGGA (SEQ ID: 3) is similar to the standard ribosome binding site of Shine-Dalgarno, AAGGAG, it is not obvious for one skilled in the art that SEQ ID NO:3 will be an efficient ribosome binding site as well.

Any comments considered necessary by applicant must be submitted no later then the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Art Unit 1652

Patent examiner

; they also did not express the modified enzyme in a zinc resistant microorganism and zinc containing medium, i.e. under conditions that increase activity of the expressed enzyme.

. The modified gene is expressed in a zinc tolerant organism, providing for higher activity of the expressed enzyme which depends on zinc. D-aminoacylase is an enzyme useful industrially for production of D-amino acids of high optical purity.

REBECCA E. PROUTY
PRIMARY EXAMINER
~~GROUP 1800~~
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